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☐ 11. Document ID: US 5994128 A

L2: Entry 11 of 11 File: USPT Nov 30, 1999

US-PAT-NO: 5994128
DOCUMENT-IDENTIFIER: US 5994128 A

TITLE: Packaging systems for human recombinant adenovirus to be used in gene therapy

DATE-ISSUED: November 30, 1999

US-CL-CURRENT: 435/325; 424/93.21, 435/320.1, 435/455, 435/69.1, 536/23.1

APPL-NO: 08/ 793170 [PALM]
DATE FILED: March 25, 1997

PARENT-CASE:
RELATED APPLICATIONS This patent application is a National Stage application under 35 U.S.C. .sctn.371 of International patent Application PCT/NL96/00244 filed on Jun. 14, 1996 which itself claims priority from European patent application 95201728.3 filed on Jun. 26, 1995 and European patent application 95201611.1 filed on Jun. 15, 1995.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
EP	95201611	June 15, 1995
EP	95201728	June 26, 1995

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/NL96/00244	June 14, 1996	WO97/00326	Jan 3, 1997	Mar 25, 1997	Mar 25, 1997

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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L2: Entry 9 of 11 File: USPT Jul 24, 2001

US-PAT-NO: 6265212
DOCUMENT-IDENTIFIER: US 6265212 B1

TITLE: Packaging systems for human recombinant adenovirus to be used in gene therapy

DATE-ISSUED: July 24, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fallaux; Frits J.	Leiderdorp			NL
Hoeben; Robert C.	Leiden			NL
Bout; Abraham	Moerkapelle			NL
Valerio; Domenico	Leiden			NL
van der Eb; Alex J.	Oegstgeest			NL
Schouten; Govert	Leiden			NL

US-CL-CURRENT: 435/320.1; 424/93.21, 435/235.1, 435/325, 435/69.1, 536/23.1

CLAIMS:

What is claimed is:

1. A method of making replication-defective adenovirus lacking functional adenoviral E1A and E1B proteins comprising a) providing a primary cell comprising a first nucleic acid sequence encoding functional E1A protein and E1B protein but not pIX protein; b) transfecting said cell with a second nucleic acid sequence comprising at least one functional adenoviral encapsidating signal and at least one functional adenoviral inverted terminal repeat, wherein said second nucleic acid sequence does not encode functional adenoviral E1A or E1B; and further wherein said first and second nucleic acids sequences lack overlapping sequences, the overlapping sequences otherwise enabling homologous recombination leading to replication competent adenovirus in said cell; c) culturing the transfected cell; and d) harvesting replication-defective adenovirus lacking functional adenoviral E1A and E1B from the cultured cell.

2. The method according to claim 1, wherein said second nucleic acid sequence is in linear form and comprises functional Inverted Terminal Repeats at or near both termini.

3. The method according to claim 1, wherein said second nucleic acid sequence is DNA.

4. The method according to claim 1, wherein the first or second nucleic acid sequence comprises a mutation in the E2A adenoviral gene that encodes a temperature sensitive gene product.

5. The method of claim 1, wherein the primary cell is of human origin.

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L2: Entry 1 of 11 File: USPT Aug 5, 2003

US-PAT-NO: 6602706
DOCUMENT-IDENTIFIER: US 6602706 B1

TITLE: Packaging systems for human recombinant adenovirus to be used in gene therapy

DATE-ISSUED: August 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fallaux; Frits Jacobus	Leiderdorp			NL
Hoeben; Robert Cornelis	Leiden			NL
Van Der Eb; Alex Jan	Oegstgeest			NL
Bout; Abraham	Moerkapelle			NL
Valerio; Domenico	Leiden			NL

US-CL-CURRENT: 435/325; 435/320.1, 435/455, 435/69.1, 435/91.4

CLAIMS:

What is claimed is:

1. An established adenovirus packaging cell comprising a first nucleic acid sequence consisting of a nucleic acid sequence encoding an adenoviral E1A region gene product and a constitutive promoter controlling said nucleic acid sequence encoding said adenoviral E1 A region gene product, said established adenovirus packaging cell further comprising: one or more recombinant nucleic acid molecules lacking overlapping sequences with the first nucleic acid sequence of said established adenovirus packaging cell, the overlapping sequences otherwise enabling homologous recombination leading to replication competent virus in said established adenovirus packaging cell.

2. The established adenovirus packaging cell of claim 1, wherein said established adenovirus packaging cell does not express E1B products.

3. The established adenovirus packaging cell of claim 1, wherein the genetic information encoding E1B products is absent.

4. The established adenoviris packaging cell of claim 1, further comprising a marker gene.

5. The established adenovirus packaging cell of claim 4, wherein said marker gene is under control of an E1 B responsive promoter.

6. The established adenovirus packaging cell of claim 1, wherein said established adenovirus packaging cell does not express a 21 kDa E1B product.

7. The established adenovirus packaging cell of claim 1, wherein genetic information encoding a 21 kDa E1B product is not present.

8. The established adenovirus packaging cell of claim 1, wherein said established adenovirus packaging cell is a diploid cell.

9. The established adenovirus packaging cell of claim 1, wherein said established adenovirus packaging cell is of non-human origin.

10. The established adenovirus packaging cell of claim 1, wherein said established adenovirus packaging cell is of monkey origin.

11. An established adenovirus packaging cell comprising a first nucleic acid sequence consisting of a nucleic acid sequence encoding an adenoviral E1A region gene product and said established adenovirus packaging cell further comprising a nucleic acid sequence encoding an adenoviral E2A region gene product under the control of an inducible promoter, said established adenovirus packaging cell further comprising: one or more recombinant nucleic acid molecules lacking overlapping sequences with the first nucleic acid sequence of said established adenovirus packaging cell, the overlapping sequences otherwise enabling homologous recombination leading to replication competent virus in said established adenovirus packaging cell.

12. The established adenovirus packaging cell of claim 11, wherein the nucleic acid sequence encoding the adenoviral E2A region gene product is mutated to alter the host range of the adenovirus as compared to wild-type adenovirus.

13. The established adenovirus packaging cell of claim 11, wherein said established adenovirus packaging cell does not express E1B products.

14. The established adenovirus packaging cell of claim 11, wherein the genetic information encoding E1B products is absent.

15. The established adenovirus packaging cell of claim 11, wherein said established adenovirus packaging cell does not express a 21 kDa E1B product.

16. The established adenovirus packaging cell of claim 11, wherein genetic information encoding a 21 kDa E1B product is not present.

17. The established adenovirus packaging cell of claim 11, wherein said established adenovirus packaging cell is a diploid cell.

18. The established adenovirus packaging cell of claim 11, wherein said established adenovirus packaging cell is of non-human origin.

19. The established adenovirus packaging cell of claim 18, wherein said established adenovirus packaging cell is of monkey origin.

20. An established adenovirus packaging cell comprising a first nucleic acid sequence consisting of a nucleic acid sequence encoding an adenoviral E1A region gene product and said established adenovirus packaging cell further comprising a nucleic acid sequence encoding an adenoviral E2A region gene product having a ts125 mutation, said established adenovirus packaging cell further comprising: one or more recombinant nucleic acid molecules lacking overlapping sequences with the first nucleic acid sequence, the overlapping sequences otherwise enabling homologous recombination leading to replication competent virus in said established adenovirus packaging cell.

21. The established adenovirus packaging cell of claim 20, wherein said established adenovirus packaging cell does not express E1B products.

22. The established adenovirus packaging cell of claim 20, wherein the genetic information encoding E1B products is absent.

23. The established adenovirus packaging cell of claim 20, wherein said established adenovirus packaging cell does not express a 21 kDa E1B product.

24. The established adenovirus packaging cell of claim 20, wherein genetic information encoding a 21 kDa E1B product is not present.

25. The established adenovirus packaging cell of claim 20, wherein said

established adenovirus packaging cell is a diploid cell.

26. The established adenovirus packaging cell of claim 20, wherein said established adenovirus packaging cell is of non-human origin.

27. The established adenovirus packaging cell of claim 26, wherein said established adenovirus packaging cell is of monkey origin.

28. The established adenovirus packaging cell of claim 20, wherein the nucleic acid sequence encoding the adenoviral E2A region gene product is mutated to alter the host range of the adenovirus as compared to wild-type adenovirus.